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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/075,404	02/13/2002	Ben F. Johnson	5010-306-01	8150

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EXAMINER

NOGUEROLA, ALEXANDER STEPHAN

ART UNIT	PAPER NUMBER
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1753

DATE MAILED: 05/04/2006

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary

Application No.

10/075,404

Applicant(s)

JOHNSON ET AL.

Examiner

ALEX NOGUEROLA

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-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on 07 March 2006.
- 2a) ☐ This action is **FINAL**. 2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 23-40 is/are pending in the application.
- 4a) Of the above claim(s) _____ is/are withdrawn from consideration.
- 5) ☐ Claim(s) _____ is/are allowed.
- 6) ☒ Claim(s) 23-40 is/are rejected.
- 7) ☐ Claim(s) _____ is/are objected to.
- 8) ☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☒ The drawing(s) filed on 13 February 2002 is/are: a) ☒ accepted or b) ☐ objected to by the Examiner.
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some * c) ☐ None of:
- ☐ Certified copies of the priority documents have been received.
 - ☐ Certified copies of the priority documents have been received in Application No. _____.
 - ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

- ☒ Notice of References Cited (PTO-892)
- ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
- ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08)
Paper No(s)/Mail Date _____.
- ☒ Interview Summary (PTO-413)
Paper No(s)/Mail Date. _____.
- ☐ Notice of Informal Patent Application (PTO-152)
- ☐ Other: _____.

DETAILED ACTION

Status of Rejections pending since the Office action of October 11, 2005

1. All previous rejections are withdrawn.

Claim Rejections - 35 USC § 112

2. Claims 30-32 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention:

- a) Claim 30 recites the limitation "electric ramp" in line 3. There is insufficient antecedent basis for this limitation in the claim.

3. Note that dependent claims will have the deficiencies of base and intervening claims.

Claim Rejections - 35 USC § 102

4. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless –

(b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

5. Claims 24 and 33-37 are rejected under 35 U.S.C. 102(b) as being anticipated by Guttman (US 5,296,116) ("Guttman").

Addressing claim 24, Guttman discloses a capillary method in which analyte species are separated by differential electrophoretic migration through a fluid separation medium under the influence of a run field, an improvement for reducing peak broadening caused when the run field is established comprising

establishing the run field at a ramp rate no greater than about 5V/cm-s (Figure 3 and col. 7:33-36 – ramp rate is 400 V/cm in 20 minutes or 0.33 V/cm-s);

wherein the analyte species are nucleic acid (col. 7:33-37 and col. 5:13-20).

Applicants should note that the "run field" is not required by the claim to be constant nor different from the ramp rate by which it is established. In Guttman the ramp rate is the same as the run field; that is, 0.33V/cm-s.

Addressing claims 33-37, note again in Guttmman ramp rate = run field and the electrical field used is 400 V/cm in 20 minutes or 0.33 V/cm-s.

Claim Rejections - 35 USC § 103

6. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

7. The factual inquiries set forth in *Graham v. John Deere Co.*, 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. 103(a) are summarized as follows:

1. Determining the scope and contents of the prior art.
2. Ascertaining the differences between the prior art and the claims at issue.
3. Resolving the level of ordinary skill in the pertinent art.
4. Considering objective evidence present in the application indicating obviousness or nonobviousness.

8. This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

9. Claims 23 and 25-29 are rejected under 35 U.S.C. 103(a) as being unpatentable over Guttman (US 5,296,116) ("Guttman") over Dubrow (US 5,164,055) ("Dubrow").

Guttman discloses a capillary method in which analyte species are separated by differential electrophoretic migration through a fluid separation medium under the influence of a run field, an improvement for reducing peak broadening caused when the run field is established comprising

establishing the run field at a ramp rate no greater than about 5V/cm-s (Figure 3 and col. 7:33-36 – ramp rate is 400 V/cm in 20 minutes or 0.33 V/cm-s);

wherein the fluid separation is a buffered solution containing a crosslinked polymer and the analyte species are nucleic acid (col. 7:33-37 and col. 5:13-20).

Applicants should note that the “run field” is not required by the claim to be constant nor different from the ramp rate by which it is established. In Guttman the ramp rate is the same as the run field; that is, 0.33V/cm-s.

Dubrow discloses non-crosslinked polymers for capillary electrophoresis separation of nucleic acids. See the abstract and col. 3:58 – col. 4:2.

It would have been obvious to one with ordinary skill in the art at the time of the invention to use a non-crosslinked polymer as taught by Dubrow in the invention of Guttman because as taught by Dubrow “... the resolution achievable in the medium is significantly improved over prior art high-concentration gel –electrophoresis methods, by virtue of the greater homogeneity and lack of voids in the medium.” See col. 11:30-35.

Addressing claims 25-29, note again in Guttman ramp rate = run field and the electrical field used is 400 V/cm in 20 minutes or 0.33 V/cm-s.

10. Claims 30-32 are rejected under 35 U.S.C. 103(a) as being unpatentable over Guttman (US 5,296,116) ("Guttman") and McCormick ("Capillary Zone Electrophoretic Separation of Peptides and Proteins Using Low pH Buffers in Modified Silica Capillaries," *Anal. Chem.* 1988, 60, 2322-2328).

Guttman discloses a capillary method in which analyte species are separated by differential electrophoretic migration through a fluid separation medium under the influence of a run field, an improvement for reducing peak broadening caused when the run field is established comprising

establishing the run field at a ramp rate no greater than about 5V/cm-s (Figure 3 and col. 7:33-36 – ramp rate is 400 V/cm in 20 minutes or 0.33 V/cm-s);

wherein the analyte species are nucleic acid (col. 7:33-37 and col. 5:13-20).

Applicants should note that the "run field" is not required by the claim to be constant nor different from the ramp rate by which it is established. In Guttman the ramp rate is the same as the run field; that is, 0.33V/cm-s.

Guttman does not mention to what extent peak broadened is reduced compared to that found when an electric ramp is not used. However, Guttmann does disclose enhanced peak resolution by using an electric ramp. Barring a contrary showing, such as unexpected results, a particular percentage improvement in peak resolution is just optimization, which Guttmann also discloses, especially since Guttmann meets the claimed ramp rate range. See col. 8:30-39 and col. 2:14-22 and the rejection of claim 23.

Although not needed to meet this claim, assuming that “electric ramp” is somehow limited to just the initial field soon after sample injection (which is anyway included by Guttman in his ramping), it was also known at the time of the invention how to evaluate the effect of different ramp rates on separation resolution. See in McCormick the abstract; Electrophoresis on page 2322; Figure 1; Figure 12; and the second full paragraph in the first column on page 2327. It was further known to use a ramp rate of no greater than 5V/(cm-s). See the passages already cited in McCormick and note that McCormick discloses a capillary electrophoresis method using a ramp rate of 0.70 V/(cm-s) (capillary length = 110 cm, run voltage = 23kV (from injection voltage of 2kV), and rise time = 300s). Although McCormick does not mention using a non-crosslinked polymer or separating nucleic acids McCormick is relevant because he does disclose coating the inside of the capillary with polymer and separating biomolecules (proteins) and believes that using an electric ramp may be useful for a variety of samples since he states

“Another factor that strongly influences the quality of CZE separations is the rate at which the voltage is applied across the capillary at the start of the separation,” and

“... it is suspected that it [the separation efficiency improvement] derives from establishment of equilibrium conditions (thermal, ionic, etc.) in the capillary as the voltage is imposed at the start of the separation ... gradual rather than instantaneous imposition of the running voltage apparently results in reduced broadening of the

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sample zone by allowing the electrosmotic flow, capillary temperature, double-layer characteristics, etc. to slowly attain equilibrium conditions.”

See the abstract; Capillary Modification on page 2322; first sentence in the second full paragraph in the first column on page 2327, and the second column on page 2327.

11. Claims 39-40 are rejected under 35 U.S.C. 103(a) as being unpatentable over Guttman (US 5,296,116) (“Guttman”) over Dubrow (US 5,164,055) (“Dubrow”) as applied to claims 23 and 25-29 above, and further in view of McCormick (“Capillary Zone Electrophoretic Separation of Peptides and Proteins Using Low pH Buffers in Modified Silica Capillaries,” *Anal. Chem.* 1988, 60, 2322-2328).

Guttman does not mention to what extent peak broadened is reduced compared to that found when an electric ramp is not used. However, Guttmann does disclose enhanced peak resolution by using an electric ramp. Barring a contrary showing, such as unexpected results, a particular percentage improvement in peak resolution is just optimization, which Guttmann also discloses, especially since Guttmann meets the claimed ramp rate range. See col. 8:30-39 and col. 2:14-22 and the rejection of claim 23.

Although not needed to meet this claim, assuming that “electric ramp” is somehow limited to just the initial field soon after sample injection (which is anyway included by Guttman in his ramping), it was also known at the time of the invention how to evaluate the effect of different ramp rates on separation resolution. See in McCormick the abstract; Electrophoresis on page 2322; Figure 1; Figure 12; and the second full paragraph in the first column on page 2327. It was further known to use a ramp rate of no greater than $5\text{V}/(\text{cm}\cdot\text{s})$. See the passages already cited in McCormick and note that McCormick discloses a capillary electrophoresis method using a ramp rate of $0.70\text{ V}/(\text{cm}\cdot\text{s})$ (capillary length = 110 cm, run voltage = 23kV (from injection voltage of 2kV), and rise time = 300s). Although McCormick does not mention using a non-crosslinked polymer or separating nucleic acids McCormick is relevant because he does disclose coating the inside of the capillary with polymer and separating biomolecules (proteins) and believes that using an electric ramp may be useful for a variety of samples since he states

“Another factor that strongly influences the quality of CZE separations is the rate at which the voltage is applied across the capillary at the start of the separation,” and

“... it is suspected that it [the separation efficiency improvement] derives from establishment of equilibrium conditions (thermal, ionic, etc.) in the capillary as the voltage is imposed at the start of the separation ... gradual rather than instantaneous imposition of the running voltage apparently results in reduced broadening of the

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sample zone by allowing the electrosmotic flow, capillary temperature, double-layer characteristics, etc. to slowly attain equilibrium conditions."

See the abstract; Capillary Modification on page 2322; first sentence in the second full paragraph in the first column on page 2327, and the second column on page 2327.

12. Any inquiry concerning this communication or earlier communications from the examiner should be directed to ALEX NOGUEROLA whose telephone number is (571) 272-1343. The examiner can normally be reached on M-F 8:30 - 5:00.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, NAM NGUYEN can be reached on (571) 272-1342. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).



Alex Noguera
Primary Examiner
AU 1753
April 28, 2006